

EXHIBIT B

Part 1 of 2

**Lupin's Argument re
Likelihood of Success on the Merits**

December 2, 2011

Sciele Pharma, Inc., et al. v. Lupin Ltd., et al.

C.A. No. 09-037

Summary of Lupin's Arguments

Infringement

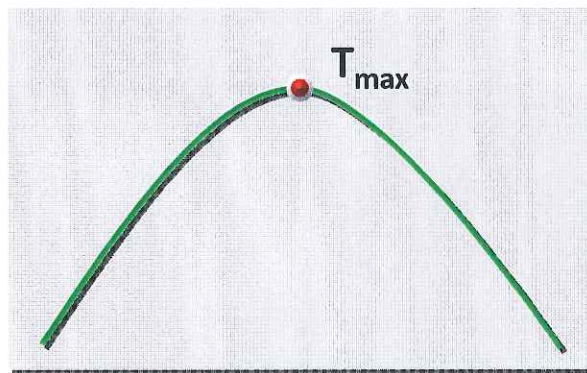
- After-dinner study on Lupin's product gave $T_{\max} \geq 12$ hours
- Plaintiff's reliance on Lupin's after-breakfast study is misplaced
 - Patent claims limited to after dinner
 - Lupin's T_{\max} is two hours longer than that of Fortamet®
- Inclusion of Fortamet® data in Lupin's package insert is not an admission of patent infringement

Validity

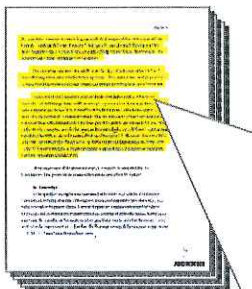
- Plaintiff is suing here on patent claims that nobody involved in the patent prosecution meant to be in the issued patent
- Lupin's obviousness defense is bolstered by intervening Supreme Court precedent

The Patent Claims as Issued Are Limited to Compositions Providing T_{\max} = 5.5 to 7.5 Hours *After Dinner*

- ✦ Closest prior art (Cheng) disclosed an identical embodiment except for extra laser-drilled hole that shortened after-dinner T_{\max} from 8 to 12 hours to 5.5 to 7.5 hours
- ✦ Cheng gave mean T_{\max} of 6.67 to 6.80 hours **after breakfast**
- ✦ When broader claims were rejected, patent owner amended the claims to be limited to administering drug **after dinner**



Only Relevant T_{max} Is 'Following Dinner'



delivered to the Examiner, the mean T_{max} values for the Examples of the '859 were as follows: Example 1 (fasting) 4.67 hours; Example 2 (fasting) 4.33 hours; Example 2 (fed a.m.) 6.80 hours; Example 3 (fed a.m.) 6.67 hours; Example 3 (Fed p.m.) 9.67 hours. Therefore, the only instance was Example 3 fed in the P.M. (at dinner).

The claims have now been amended to state the " T_{max} of metformin at from 5.5 to 7.5 hours after single dose administration following dinner." The claims as now written are directed to methods and treatments which were never accomplished in the Examples of the '859 patent.

With respect to the Examiner's position that the provided examples of the present application set forth dosage forms made according to a process where the dosage forms have the same composition as those of U.S. 6,099,859 ('859), the Examiner's attention is respectfully directed to the fact that the formulations exemplified and tested in the present application are indeed different as the formulations of the Examples of the present application differ from those of the '859 by having two laser drilled holes, and the method achieved a different result than that reported in the '859 or achieved by clinical testing of Examples 1-3. However, it is respectfully submitted that one skilled in the art would be able to manipulate the processes and formulations of the '859 by other methods to obtain the claimed pharmacokinetic parameters of the present invention by routine experimentation.

A Major Focus of Patent Is Effect After Dinner

“Plaintiffs’ ’866 patent indicates that Fortamet® is designed to provide the controlled release of an antihyperglycemic drug, with peak levels of the drug coinciding with the body’s production of peak levels of glucose. The parties all agree that Plaintiffs’ drug achieves that goal when administered at dinnertime.”

Markman Opinion at 13

Plaintiff's Reliance on Lupin's After-Breakfast Study Is Misplaced for Two Reasons

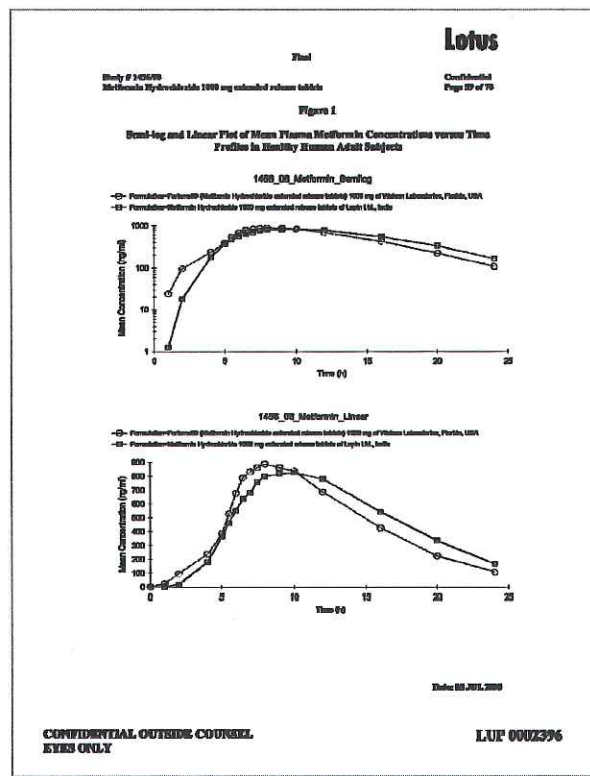
- 1. Claims are expressly limited to "following dinner"**
- 2. Lupin's breakfast study disproves Plaintiff's argument, based on the following chart, that T_{\max} profiles of Lupin's product and Fortamet[®] are "nearly identical"**

Reply Brief at 8

Plaintiff Only Reproduced One of the Two Graphs on This Page of Lupin's ANDA

Logarithm

Linear



Logarithms

$$1,000 = 10 \times 10 \times 10 = 10^3 \Rightarrow \text{Log } 3$$

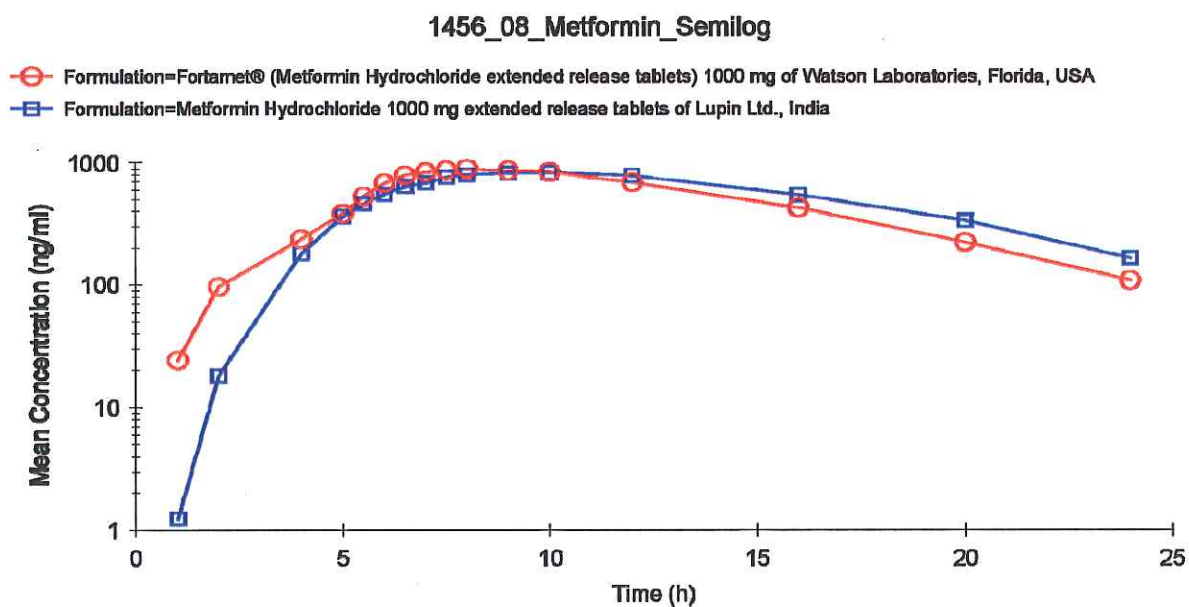
$$100 = 10 \times 10 = 10^2 \Rightarrow \text{Log } 2$$

$$10 = 10 = 10^1 \Rightarrow \text{Log } 1$$

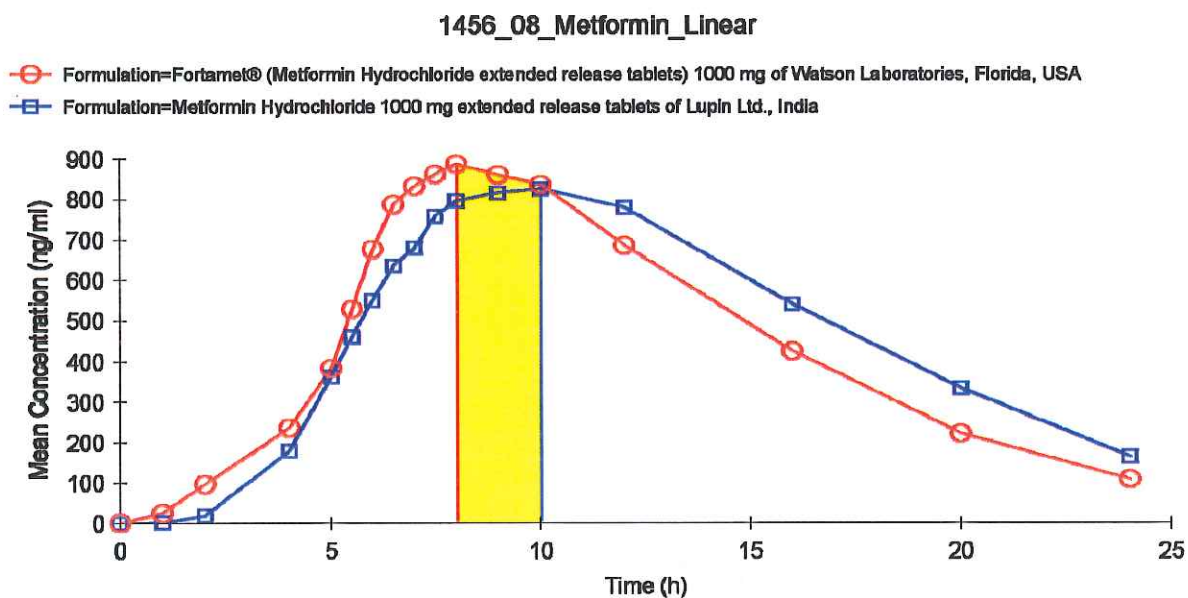
$$1 = 10^0 \Rightarrow \text{Log } 0$$

✚ Log scale means equal distance for each factor of 10 in vertical direction

Logarithm

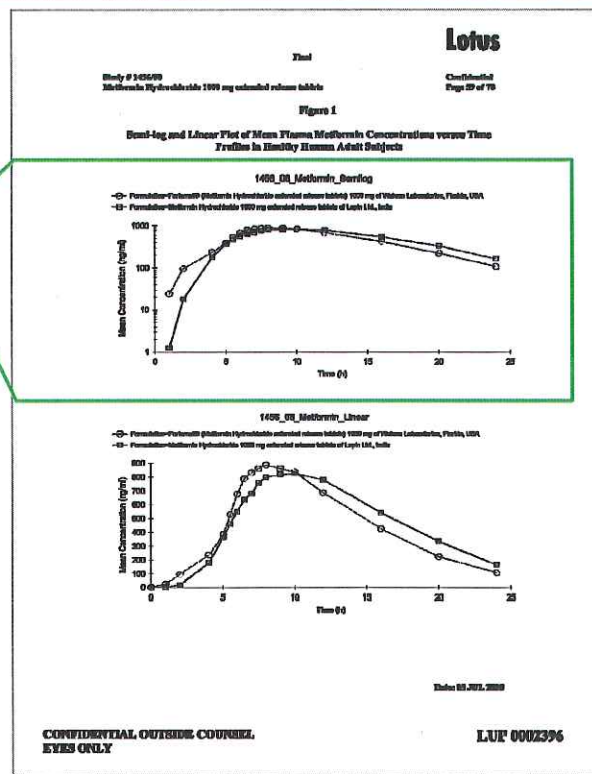


Linear



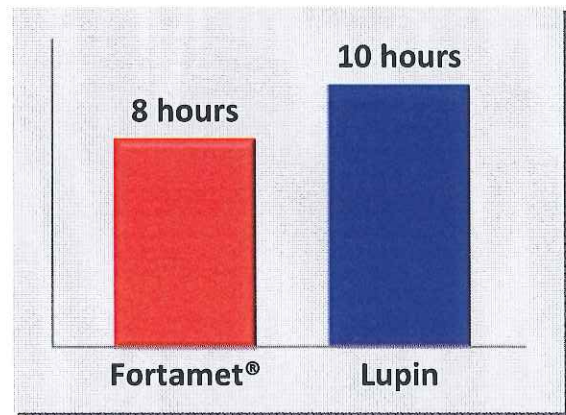
Plaintiff Only Reproduced One of the Two Graphs on This Page of Lupin's ANDA

Plaintiff Cited



Lupin's T_{\max} Is Different From That of Fortamet®

- Actual data reported in ANDA (LUP 2394-95)
- Fortamet® T_{\max} = 8.0 hours
- Lupin T_{\max} = 10.0 hours



- Disproves Plaintiff's expert assertion that the two products "have almost an identical T_{\max} "

Fleckenstein Supp. Decl., ¶ 47

Like Prior Art, Lupin's Product Has Longer T_{\max} After Dinner

- ✿ Only after-dinner test of Lupin's product gives T_{\max} of 12 hours
- ✿ Plaintiff's opening papers recite about a half-dozen criticisms, all answered in Lupin's opposition brief
- ✿ Plaintiff's reply papers raise a new half-dozen criticisms, all immaterial to whether Lupin's product has a T_{\max} of 5.5 to 7.5 hours
- ✿ Dr. Alexander Shepherd concluded that the study is scientifically valid proof of a non-infringing T_{\max}

Plaintiff's Expert Criticisms Are Immaterial or Less

- ✦ FDA approved Lupin's after-breakfast study and the bioanalytical methods Lupin used
 - ✦ FDA specifies using glucose
- ✦ Several of the criticisms of Lupin's after-dinner study center on food, but see *King Pharma, Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1275 (Fed. Cir. 2010) (where patent claim does not specify type of food, improper to read in limitations on type of food)
- ✦ None of the criticisms can fairly be said to be evidence of a T_{\max} of 5.5 to 7.5 hours

Conclusions From the Tests of Lupin's Product

Conclusions

- Lupin's product gives a non-infringing T_{\max} after dinner
- Lupin's product has a different T_{\max} from Fortamet®

Lupin's Package Insert Is Not An Admission of Infringement

- ✱ **Wrong** test (single dose vs. multidose)
- ✱ **Wrong** product (results copied from Fortamet® package)
- ✱ Case law cited by Plaintiff is distinguishable or effectively overruled by *Pliva*

Package Insert

LUPIN LIMITED

Module 1

APPROVED PACKAGE INSERT

Pharmacokinetic Parameters (mean \pm SD)	FORTAMET® 2000 mg (administered q.d. after dinner)	Immediate-Release Metformin 2000 mg (1000 mg b.i.d.)
AUC _{0-24 hr} (ng·hr/mL)	26,811 \pm 7055	27,371 \pm 5,781
T _{max} (hr)	6 (3-10)	3 (1-8)
C _{min} (ng/mL)	2849 \pm 797	1820 \pm 370

PROPOSED PACKAGE INSERT

Pharmacokinetic Parameters (mean \pm SD)	Metformin Extended - Release Tablets 2000 mg (administered q.d. after dinner)	Immediate-Release Metformin 2000 mg (1000 mg b.i.d.)
AUC _{0-24 hr} (ng·hr/mL)	26,811 \pm 7055	27,371 \pm 5,781
T _{max} (hr)	6 (3-10)	3 (1-8)
C _{min} (ng/mL)	2849 \pm 797	1820 \pm 370

Table 1 FORTAMET® Metformin Parameters at 4 Weeks		Table 1 Metformin Extended-Release Metformin Parameters at 4 Weeks	
Pharmacokinetic Parameters (mean \pm SD)	Fortamet® 2000 mg (administered q.d. after dinner)	Metformin Extended-Release Tablets 2000 mg (administered q.d. after dinner)	Metformin Immediate-Release Tablets 1000 mg (administered b.i.d.)
AUC _{0-24 hr} (ng·hr/mL)	26,811 \pm 7055	26,811 \pm 7055	27,371 \pm 5,781
T _{max} (hr)	6 (3-10)	6 (3-10)	3 (1-8)
C _{min} (ng/mL)	2849 \pm 797	2849 \pm 797	1820 \pm 370

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CONFIDENTIAL OUTSIDE COUNCIL
EYES ONLY

LUP 0000125

Package Insert

LUPIN LIMITED		Module 1
PRODUCT: METFORMIN HYDROCHLORIDE EXTENDED-RELEASE TABLETS		CHUGANALANDA-200
Section	1.14 - Labeling	
Subsection	1.14.3 - Label Drug Labeling	
Sub-subsection	1.14.3.1 - Assisted Comparison Label Drug	
1.0 SIDE BY SIDE COMPARISON OF PACKAGE INSERT (CONTINUED)		
APPROVED PACKAGE INSERT		PROPOSED PACKAGE INSERT

APPROVED PACKAGE INSERT

When **FORTAMET®** was administered with food, C_{max} was increased by approximately 30% and T_{max} was more prolonged compared with the fasting state (6.1 versus 4.0 hours).

PROPOSED PACKAGE INSERT

When metformin hydrochloride extended-release tablets was administered with food, C_{max} was increased by approximately 30% and T_{max} was more prolonged compared with the fasting state (6.1 versus 4.0 hours).

When administered with food, the pharmacokinetics of metformin as assessed by AUC₀₋₂₄ appeared to be similar to the fasting state. The extent of metformin absorption (as assessed by AUC₀₋₂₄) was increased by approximately 30% when given with food. When administered with food, C_{max} was increased by approximately 30% and T_{max} was more prolonged compared with the fasting state (6.1 versus 4.0 hours).

When administered with food, the pharmacokinetics of metformin as assessed by AUC₀₋₂₄ appeared to be similar to the fasting state. The extent of metformin absorption (as assessed by AUC₀₋₂₄) was increased by approximately 30% when given with food. When administered with food, C_{max} was increased by approximately 30% and T_{max} was more prolonged compared with the fasting state (6.1 versus 4.0 hours).

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CONFIDENTIAL OUTSIDE COUNSEL
EYES ONLY

LUP 0000126

Table 1 Does Not Address Infringement

- Test is on Fortamet[®] product, not on Lupin's product
- Describes result after "4 weeks of treatment" where "steady-state" was achieved

The Issue of Multidose Versus Single Dose Was Seemingly Resolved at Markman

- Plaintiff said a “single dose” was giving all of the drug at one time:
 - “The total amount of a drug taken at one time is essentially what plaintiffs’ position is.” (Tr. 135:22-23)
- Mylan raised the concern that “single dose” could morph into doses given over several days:
 - “[T]he real issue is when we’re interpreting that claim, are we really talking about a...drug concentration that’s in the body from the dose that the patient took this morning, or are we talking about some amount that might be left over from the day before or a couple days before? ... [W]e think the claim is talking about administration of that one dose of that particular day....” (Tr. 163:3-8, 10-12)